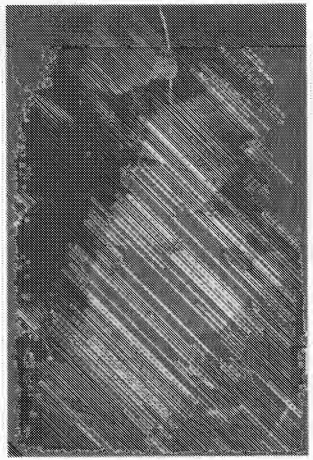
Photodynamic therapy

From Wikipedia, the free encyclopedia

Photodynamic therapy (PDT), matured as a feasible medical technology in the 1980's at several institutions throughout the world, is a ternary treatment for cancer involving three key components: a photosensitizer, light, and tissue oxygen. It is also being investigated for treatment of psoriasis and acne, and is an approved treatment for wet macular degeneration. The German physician Friedrich Meyer-Betz performed the first study with photodynamic therapy (PDT) with porphyrins in humans in 1913. Meyer-Betz tested the effects of haematoporphyrin-PDT on his own skin. Modern day versions of it were tested at the Mayo Clinic and Roswell Park Cancer Center, but did not really become widespread until Thomas Dougherty initiated clinical trials and formed the International Photodynamic Association (http://www.pms.ac.uk/ipa/index.php), in 1986.



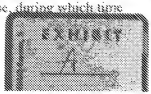
Shown is close up of surgeons' hands in an operating room with a "beam of light" traveling along fiber optics for photodynamic therapy. Its source is a laser beam which is split at two different stages to create the proper "therapeutic wavelength". A patient would be given a photo sensitive drug (photofrin) containing cancer killing substances which are absorbed by cancer cells. During the surgery, the light beam is positioned at the tumor site, which then activates the drug that kills the cancer cells, thus photodynamic therapy (PDT).

A **photosensitizer** is a chemical compound that can be excited by light of a specific wavelength. This excitation uses visible or near-infrared light.

In photodynamic therapy, either a photosensitizer or the metabolic precursor of one is administered to the patient. The tissue to be treated is exposed to light suitable for exciting the photosensitizer. Usually, the photosensitizer is excited from a ground singlet state to an excited singlet state. It then undergoes intersystem crossing to a longer-lived excited triplet state. One of the few chemical species present in tissue with a ground triplet state is molecular oxygen. When the photosensitizer and an oxygen molecule are in proximity, an energy transfer can take place that allows the photosensitizer to relax to its ground singlet state, and create an excited singlet state oxygen molecule. **Singlet oxygen** is a very aggressive chemical species and will very rapidly react with any nearby biomolecules. (The specific targets depend heavily on the photosensitizer chosen.) Ultimately, these destructive reactions will result in cell killing through apoptosis or necrosis.

As an example, consider PDT as a treatment for basal cell carcinoma (BCC). BCC is the most common form of skin cancer in humans. Conventional treatment of BCC involves surgical excision, cryogenic treatment with liquid nitrogen, or localized chemotherapy with 5-fluorouracil or other agents. A PDT treatment would involve the following steps.

- A photosensitizer precursor (aminolevulinic acid (ALA) or methyl aminolevulinate) is applied
- A waiting period of a few hours is allowed to elapse, during which time



    - ALA will be taken up by cells, and
    - ALA will be converted by the cells to protoporphyrin IX, a photosensitizer (see Porphyrin).
- The physician shines a bright red light (from an array of light-emitting diodes or a diode laser) on the area to be treated. The light exposure lasts a few minutes to a few tens of minutes.
    - Protoporphyrin IX absorbs light, causing it to an excited singlet state;
    - Intersystem crossing occurs, resulting in excited triplet protoporphyrin IX;
    - Energy is transferred from triplet protoporphyrin IX to triplet oxygen, resulting in singlet (ground state) protoporphyrin IX and excited singlet oxygen;
    - Singlet oxygen reacts with biomolecules, fatally damaging some cells in the treatment area.
- Within a few days, the exposed skin and carcinoma will scabs over and flakes away.
- In a few weeks, the treated area has healed, leaving healthy skin behind. For extensive malignancies, repeat treatments may be required. It is also common to experience pain from the area treated.
- After the treatment the patient will need to avoid excessive exposure to sunlight for a period of time.

Specificity of treatment is achieved in three ways. First, light is delivered only to tissues that a physician wishes to treat. In the absence of light, there is no activation of the photosensitizer and no cell killing. Second, photosensitizers may be administered in ways that restrict their mobility. In our example, ALA was only applied to the area to be treated. Finally, photosensitizers may be chosen which are selectively absorbed at a greater rate by targeted cells. ALA is taken up much more rapidly by metabolically active cells. Since malignant cells tend to be growing and dividing much more quickly than healthy cells, the ALA targets the unhealthy cells.

Treatment of internal organs may be achieved through the use of endoscopes and fiber optic catheters to deliver light, and intravenously-administered photosensitizers. A great deal of research and clinical study is now underway to determine optimal combinations of photosensitizers, light sources, and treatment parameters for a wide variety of different cancers.

A major disadvantage of PDT is that the light needed to activate most photosensitizers can not penetrate through more than one third of an inch (1 cm) of tissue. Thus the application of PDT is limited to the treatment of tumours on or under the skin, or on the lining of some internal organs. Moreover it is less effective in treatment of large tumours and metastasis because of the same reason.

See also

- Photomedicine

External links

- http://www.dartmouth.edu/~pdt
- http://www.massgeneral.org/wellman/research/photodynamic.asp
- http://www.photobiology.com/educational/len2/ingox.html
- http://www.esp-photobiology.it/
- http://www.kurnc.edu/POL/
- http://www.pol-us.net/ASP_Home/
- http://www.bmb.leeds.ac.uk/pdt/
- http://www.photobiology.info/
- http://www.cancer.gov/cancertopics/factsheet/Therapy/photodynamic

Journals

- Photochemical and Photobiological Sciences (http://www.rsc.org/publishing/journals/PP/Article.asp?TypeofCurrentIssue)